REPORT

ON

ANIMAL VACCINATION.

BY

HENRY A. DU BOIS, Ph.B., MD., of San Rafael, California.

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This report resolves itself into two parts. First, a brief consideration of animal vaccination; and second, a statement of what has been so far done at the only vaccine station on the Pacific Coast.*

ANIMAL VACCINATION.

It is now ninety-four years since Edward Jenner vaccinated James Phipps with virus taken from the hands of Sarah Nelmes, and tested the protection thus given the former by inoculation with smallpox virus, without effect. Since this event, an event ever to be remembered in the science of preventive medicine, virus has been taken from children and used for the protection of the inhabitants of every civilized country from the ravages of smallpox. Almost from the date of the discovery doubt was thrown on the protection thus given. Jenner believed that it lasted throughout life, and inoculations thirty years later than the original vaccinations were certainly, in many cases at least, unsuccessful; while if we give credence to the reports of certain public vaccinators, who report 80 to 90 per cent of secondary vaccinations as successful, our opinion must be that the protection given by this operation is limited to a very few years at most. The general opinion of those competent to form an unbiased judgment, from an impartial study of all the facts, seems to be that the protection lasts in some cases for life, but more often diminishes as time goes on, so that it fails to give efficient protection after a certain time, which varies in each individual case. Almost all authorities agree now in advising revaccination; some once, while most consider repetitions of the operation at various ages more prudent, if not absolutely necessary to give full protection. There are, however, some able men who still maintain that the protection given by this operation, if properly performed with virus taken directly from the cow, or only a few removes from its origin, and at once introduced into the system of the recipient, is practically for life in most cases, and found their opinion on the following facts: Jenner's vaccinations, and those of his immediate followers, were generally tested after a longer or shorter time by inoculation, and almost uniformly without success. Since this period statistics show that smallpox in those periodically vaccinated is by no means uncommon, and apparently until a few years ago the percentage of those thus becoming diseased increased steadily. This they explain by the want of proper care in the performance of the operation, and by the use of imperfect virus.

I think any one who will carefully examine the literature of the subject

*NOTE.—This report is made at the request of Dr. Orme, President of the State Board of Health of California. It was first intended to include the full consideration of the nature of virus, as well as the technique of its production, storage, and distribution, but as this plan involved a number of colored plates to make the appearances of the characteristic vesicles intelligible to the reader, which, perhaps, fortunately for him, the State was not willing to pay for, I have reserved most of the material collected relating to this portion of the subject for publication elsewhere; and have aimed here to be as brief as the subject would admit of.

will agree with me when I say that physicians generally for many years after Jenner's discovery knew more about this operation than they do now. That it was not then, with the memories of inoculation still fresh in their minds, considered a trifling one, that could be safely intrusted to any untrained operator. Jenner certainly never wearied in urging that no one should be allowed to vaccinate until he had been first properly trained. Further, I think that humanized virus can be materially improved or impaired by the physical condition of the children, through whose system it is passed, and that on the whole virus generally in use in this country fifteen years ago, before the introduction of bovine virus, showed a great difference in its effects when compared with the action of the latter, this producing vesicles resembling in character those of the classical description given by Jenner. My own opinion is that want of instruction lies at the bottom of this whole matter. The medical student of the present day really knows nothing of vaccination, and the practitioner too, generally, only what he has learned by a not too fruitful experience. I can find no positive evidence that virus must *necessarily* deteriorate by its continued passage through the human system, but there seems the strongest evidence that humanized virus in England and in this country at least, and probably in other countries also, before the introduction of animal virus had a shorter period of incubation, a less typical vesicle, a less defined areola, and caused less constitutional symptoms than in Jenner's lifetime. Certainly in comparing a personal experience of a good many thousand cases vaccinated with humanized lymph from 1861–8 with a more limited number in recent years, in which animal virus has alone been used, the difference has been marked, though one chiefly of degrees.

Statistics in England show a gradual lessening of protection, or else an increased infectiousness in smallpox. Revaccinations seem now required at shorter intervals than for some twenty to thirty years after its first introduction, at least such seems the case so far as a comparison of the effects of subsequent inoculation in early times with the apparent necessity of frequent revaccination in the present. As this test is not available we cannot, of course, ascertain with the same degree of accuracy the protection afforded. As to the frequency of revaccination, there are no statistics to enable us to determine the average period of protection with any approach to accuracy, and any regulations on this subject for the benefit of the public should, of course, be based on the least period of time, not on a general average of time that protection is given. Perhaps vaccination at three to six months after birth, at twelve years, again at twenty to twenty-five, and perhaps after forty, with revaccination at any age before or during an epidemic, would comply with the result of the experience of those who have devoted most thought to this subject.

There seems to be evidence, chiefly from Belgium, to show that by the use of animal virus as great if not greater protection can now be given than was in early times afforded by the virus first introduced by Jenner. It must be remembered that in this country animal vaccination has been largely in use for fifteen or more years. So in any comparison of the activity of these two forms of viruses, due allowance must be made for its influence on the humanized virus of the country at large. We can, in fact, in this country at least, obtain no virus humanized for a length of time to compare the animal virus with. So repeatedly have the profession gone back to the cow, that it is doubtful if a single case of cowpox can now be found in the United States, whose virus has come from Jennerian stock.

What are the advantages and disadvantages of using either virus, and which, on the whole, is preferable? We have already alluded to one

decided advantage—the greater activity of bovine virus, properly propagated and stored, when successfully introduced into the system. By this I do not wish to be understood to mean that as ordinarily used it will "take" in a greater proportion of cases. Very little experience is needed to convince one that this is the exact reverse of the truth. The introduction of a virus from one species into the system of another with a lower body temperature always presents more difficulties than in the introduction of the virus of the same species. What I mean is that *when successfully introduced* its action is more thoroughly constitutional, and the local effects are the exact counterpart of those described as typical by Jenner, and which resisted inoculation many years subsequently. I have here, I believe, presented what to my mind is the chief advantage of animal virus, as well as its chief disadvantage, its thoroughness when inoculated, and the difficulty attending its inoculation.

It may, perhaps, be well to illustrate this briefly. Buist, of Edinburgh, holding an official position as teacher of vaccination to the local Board, says, in a very excellent original work recently published, that four scratches one third of an inch long and three fourths of an inch apart, made with a needle, will, if the virus is taken from a healthy child (alongside), at the seventh day produce four good sized vesicles, causing cicatrices covering, collectively, at least half an inch square, while if the lymph is half an hour old only one or two vesicles will form, and these much smaller in size, and that to secure results equal to those of the fresh virus at least forty-eight scratches, close together, will be found to be necessary. The directions that he gives for the use of all stored virus, humanized and animal, are precise and worthy of note, especially in this State, where the "*vaccine rake*" seems the favorite instrument. The directions are there officially issued, and direct that the arm shall first be well *washed* and *rubbed* until dry and reddened. The vaccine virus is then applied and the scratches made through it with a *new* needle, so as not to draw blood. The virus is rubbed into the scratches with the eye of the needle, which is then thrown away. When primary vaccination fails, he directs the operation to be repeated with arm-to-arm lymph, as he justly says that even apparent failures are proved to exert some constitutional influence, which can only be overcome by a more active material, while in partial failures he recommends a second vaccination a few days later, which even when no vesicles result hastens the formation and increases the size of those resulting from the first vaccination. Another comparison of these two forms of virus shows that convenience may sometimes be in favor of one, and at other times of the other. Thus, with a compulsory vaccination law, strictly enforced, arm-to-arm vaccination is practicable, and can be practiced by a trained corps of vaccinators, thereby avoiding much of the danger incident to the use of humanized virus. In this country, with no such law, and with no special training required of the operators, these advantages do not exist. Arm-to-arm vaccination becomes always a troublesome operation, and often impossible, forcing us to resort to some form of stored virus. Bovine lymph, on the other hand, can always be had. Calves can be selected, and, with a thermometer, the progress of their inoculation can be watched, and only virus from typical vesicles need be taken. The quantity of virus is also under control, a very important matter during an epidemic. These are undoubtedly great advantages, but they are unfortunately nearly all neutralized in this State. The State neither owns, controls, nor exercises supervision over any vaccine station. Health Boards, unfortunately, are political bodies, their members being, as a rule, selected, not for their reputation in preventive medicine, but rather

for their political influence. Virus is supposed to be bought in the open market. The cheapest reliable article is supposed to be secured. By whom and how propagated few Health Boards or physicians ask, and if they received a full reply, are not competent to decide as to whether a virus had been propagated with due care and skill, and there is no official authority to give them this information. Virus is found in the market opposed to virus, until, as Dr. Martin truly says: "In times of great demand (the time above all others when only what is known to be the best should be purchased) certain propagators have found this method" (alluding to his method of propagating virus by numerous small single vesicles) "far too old fashioned and 'unbusiness like' for their views. An animal must be made to yield fifteen thousand to twenty thousand points, or none."

He goes on to say that a full grown cow is selected and large sores are made, which, when inoculated, give rise to compound vesicles which frequently coalesce into one or more large sores, giving out an enormous supply of colorless serum containing few vacciniads, their place being supplied by pus cells and other septic matter, the product of inflammatory action. Such virus readily produces a powerful local action, not, however, the typical vesicle; often causes deep ulceration and resulting fever; is not infrequently accompanied by a general eruption, which can be communicated to others, causing sores difficult to heal, and leaving permanent scars. Virus thus produced is *cheap*. Virus produced from single vesicles, yielding only two hundred to three hundred points to an animal, and requiring to be taken slowly, must always be dear. So long as virus is judged by the *amount* and not by the *kind* of constitutional and local irritation produced, and so long as cheapness is demanded before quality, so long will vaccinations frequently present ulcerations accompanied with high fever. Smallpox may, as in a recent case, be contracted with "a splendid sore" on the arm, and thus the distance between the office of the public vaccinator and the pesthouse may not be far. This subject will receive explanation when we come to a consideration of the vaccine microbe and its spore.

There is yet another comparison to be made; and here everything, I believe, is in favor of the use of properly prepared bovine virus. Certain diseases can be communicated by inoculating blood. Syphilis, leprosy, eczema, erysipelas, repeated experiments have shown, can thus be communicated. Tuberculosis, it is probable, can also be thus transmitted. Whether any of these diseases can be transmitted by the liquor sanguinis contained in the vaccine vesicle, and in which the solid bodies which are proved to transmit the contagion exist, is not certainly known.

Dr. Cory, of St. Thomas Hospital, London, inoculated himself with syphilis, to show that pure vaccine virus contained nothing but virus; but it is by no means certain that, with all the care which he doubtless took, that he did not also inoculate blood. Practically, blood may exist in apparently pure virus. A careful microscopic examination is the only certain method of ascertaining its absence. This, obviously, cannot be made use of every time we vaccinate a child. Therefore, with every precaution we may take, we may inoculate blood; and thereby, if not in the lymph itself, transmit another disease. Statistics fortunately show that this seldom occurs. Some twenty-four cases have been reported in England, and about three hundred on the continent. I have no information of the number that have occurred in this country. Bovine virus is entirely free from this danger. Calves rarely have tuberculosis, veterinarians state, though some varieties of cows, especially after calving, are very subject to it, the proportion, according to Dr. Law, a United States Government Inspector, being as high as one half. If the animal is slaughtered from

whom the virus is taken, and before its issue, as is done by the State in Belgium, this danger is entirely done away with.

To sum up, then, I would say that, in my opinion, bovine virus propagated for *quality* only, by a competent physician, under proper official supervision, while it presents certain objections, yet on the whole is more reliable than humanized virus. It is entirely free from the danger of producing other diseases, and much more convenient than humanized lymphs, especially in this country, for all public vaccinations. Where it fails, the virus used being known to be active, and revaccination a few days later is unsuccessful also, arm-to-arm lymph should undoubtedly be tried. To use animal virus successfully its introduction must be accomplished. A careful examination of fourteen thousand ivory points used during the late prevalence of smallpox in this State showed very considerable quantities of virus remaining on eight thousand—considerably over half, it will be seen, of the whole number—sufficient, even after the points had been washed several times in cold water and bleached by a solution of peroxide of hydrogen, to well coat the points.

To preserve virus, dryness and an even temperature below 60 degrees Fahrenheit are necessary. There is no possible objection to the thorough drying of the virus on the points, provided that the necessary care is taken to remove it all when it is used. This is easily effected by tepid water, or glycerine and water, and allowing the points to remain moist for a few minutes before using. After using it is desirable to rinse the points in water to be sure that the coating is all removed. Dr. Martin directs that the virus shall be mixed with the water on the point by means of another point or a lancet. *Failure to remove the virus is a more frequent cause of want of success with animal virus than all other causes combined.* Warlomont gives an account of using virus that had previously in other hands failed, by moistening it with glycerine and water and allowing it to remain for twenty-four hours under a glass cover in a warm room, when it proved very active. Dr. Salmon, Chief of the United States Bureau of Animal Industry, writes me that in his opinion the best way of preserving animal virus is by its thorough drying on quill or ivory points, and its subsequent protection from changes of temperature. Dr. Winslow Anderson, of San Francisco, one of the public vaccinators, tells me that he uses glycerine and water, and has recently tested some Pacific Coast vaccine and obtained a typical vesicle with a point which had been fifty days in his office. I have used successfully on calves and children virus much older than this—in one case fifty-eight days, in another ninety days, and later one hundred and fifty days—with as good results as to type of vesicles and yield of virus as I have obtained with virus a few days old, and Dr. Martin states that he has successfully used virus dried on ivory points a year old.

Passing over the history of the introduction of animal virus, as well as the technical methods on which its successful propagation depends, which latter, though simple, involves constant attention to minute details, which would be of no interest to the general practitioner, and which, to make them thoroughly understood, would require much space and a number of carefully executed plates, I come to the theoretical portion of this subject; and first, what is vaccine? How does it act on the human body so as to render it insusceptible to the contagion of smallpox? A brief statement of the present state of opinion on these subjects, and a still shorter account of the establishment of the first vaccine station on this coast, will close this report.

The active agent in vaccine virus can be separated by an earthen filter, and is found to be solid, not fluid—so much experiment seems to prove. This solid is believed to be a vegetable germ, because it has the power of reproduction, which inorganic matter has not. It is believed to be vegetable in its nature, from its close resemblance to yeast, and to certain fungi, and to be an air absorbing spore, and not a full developed microbe. While the microbe is readily cultivated in solid as well as fluid media, the spore or germ is found difficult if not impossible of reproduction outside the body. It is readily developed, however, into the mature microbe, or its development can apparently be stopped at certain stages; each of these stages seems to produce a characteristic coloration when the cultivation is made in a solid media, as in gelatine or agar-agar. These colors, so far as observed, are white, yellow, orange, and brown. The action of all of these colored cultivations, when inoculated into the system, differs greatly from that produced by the fresh virus transferred at once from arm to arm. They seem also to differ in some respects one from the other, though so far the exact differences have not been fully studied. Thus there are found a colorless virus, taken early (before the eighth day) from the vesicle; a cloudy or white virus, taken after the areola forms, and which is also produced by artificial cultivation; and the yellow, orange, and brown viruses, produced by cultivation outside the body.

It may be asked how does this spore or germ of a microbe produce a disease in man, and is the disease produced smallpox, softened and modified in its action, but essentially smallpox still, or is it a new disease which produces such changes in the human system as to unfit it to receive the germ of variola. Briefly we may say that this spore entering the system in "true vaccine," develops into the microbe by absorbing free oxygen from the cells of which the body is made up. This oxygen the cells part with, but only after a certain resistance, so that if the spores are only few in number and of feeble vitality, few succeed in developing into microbes. Most of them are starved and die. Two things happen, however, with those that live. These take oxygen from the cells for their own growth, and in doing so give out a specific toxic alkaloid or ptomaine, which in its turn, so to speak, stupefies the cells, so that they give up their oxygen with less resistance. This mutual action goes on until no more of this poisonous alkaloid is formed by the germ, because it can obtain no more free oxygen from the cells. The cells unpoisoned retain their oxygen, while without it the spore remains a spore, and does not develop into a microbe. How this ptomaine causes the cells to give up their oxygen is so far unknown. Its action seems to be upon the bioplasm—the living jelly of which all animal and vegetable life is built up.

Such is the theory advanced by Dr. Salmon, of Washington, to explain contagious diseases produced by air absorbing microbes. If true, it must be able to explain incubation, or the latency of a virus—the protection given for a longer or shorter period—together with succeeding susceptibility, as well as to account for the enormous increase of the virus in the body, and for the identity of each contagious disease. If it does all this, it must do still more, to entitle it to our belief. When we cultivate the germ outside the body in a suitable medium supplying it with oxygen, if this theory is true, it should produce a soluble alkaloid or ptomaine. If it does this, such specific ptomaine, being soluble, can be separated from the germs which produce it; and, if isolated and injected into the body, should produce such a change in the cells as is produced when it is formed within

the body by the germs themselves. Dr. Salmon claims to have cultivated the germs of hog cholera in a fluid medium to full development, and then by a certain degree of heat to have destroyed all microbes; and yet by injection of this fluid in pigeons—very insusceptible to this particular contagion—to have produced this disease. In other words, to have produced hog cholera by a soluble chemical alkaloid or ptomaine, which had previously been produced by the artificial culture of the germ of this disease outside of the body. The effect of the action of the ptomaines of various pathogenic microbes are more or less lasting on the cells, and while under their influence they are not susceptible to the particular disease, for the reason that no more spores can obtain the necessary oxygen from them to enable them to develop into microbes, and hence no more ptomaine is produced. This is, however, thought to be true only of moderate doses. Large doses seem to be able still to poison the cells and to take more oxygen from them. The cells apparently become accustomed to the action of the ptomaine, and this tolerance can be increased by successive inoculations of increasing strength, while the cells will be affected if the dose of the ptomaine is increased too rapidly. *The tolerance of the cells for the particular poison is, therefore, the cause of subsequent protection.*

A period of protection is thus accounted for, of longer or shorter duration, according to the nature of the specific microbe, as well as to the size of the dose and the thoroughness of its introduction into the system. When spores are introduced into the body, a certain time elapses before they have developed sufficiently to have poisoned the cells by their resulting ptomaine, and to take their oxygen. This period is that of incubation, while it is followed by that of the development of the symptoms of the disease. A period of fermentation thus exists, in which a poisonous alkaloid is formed, the amount of which is limited by the amount of oxygen taken from the cells, *and the process of nature to excrete this substance from the system and to repair its effects we call the disease.*

If I understand Dr. Salmon correctly, during the time from the introduction of the virus to the development of the symptoms of the disease, the spores are developing, taking oxygen and giving out their ptomaine and propagating spores. After a certain number of cells have become affected we have external manifestations of the disease. Until this period arrives the germ is said to be incubating. The period of latency is, therefore, apparent, rather than real, and only indicates that sufficient poison has not yet been formed by the microbes to cause external symptoms.

Dr. Salmon's discovery claims that the inoculation of the product of the artificial development of the germ, *after* the subsequent destruction by heat of the microbes, enables him to protect the system of an animal from the disease, and that the action of the ptomaines is milder than that of the germs themselves, as the dose can be regulated. His experiments have so far been made with pigeons, with the microbe of hog cholera, and seem conclusive as to the protection given by a number of hypodermic injections of the ptomaine solution, but he does not, so far as I can ascertain, tell us if the discharges of these pigeons were capable of communicating the disease. Unless the specific ptomaine is capable of influencing unspecific germs to take on a pathogenic action, it does not seem possible that the poison of the disease can be increased in quantity. If the pigeons give out more of the ptomaine than was introduced into their bodies, unless we assume that it acts on innocent germs in such a manner as to make them pathogenic also, the theory falls to the ground, even though protection be given by the action of the ptomaine injections.

This theory is yet new; it seems to me of exceeding promise, but before

it is fully accepted as an explanation of the phenomena, more extended experiments will have to be made. All that can be said of it at present is that it includes what seems proved to be true in the exhaustive theory of Pasteur, as well as in the ptomaine theory of Chauveau. As a valuable working hypothesis I give it, which may at no distant day become a firmly established theory, which will give us a deeper insight into contagion, together with all that that implies, viz., scientific methods of destroying the microbes in many, perhaps all, the diseases produced by specific microbic fermentation.

It would take too much space to recall the varied experiments made by Buist, Quist, and others, by which they have succeeded in propagating the microbes (and even the spores, it is claimed by the latter) of vaccinia and variola, and have thereby, to a certain extent, confirmed the earlier experiments of Ceely and Badcock, as to the identity of the viruses of these diseases, not only so far as the microscope can do so, but also so far as their cultivation in artificial media, fluid and solid, is concerned.

IDENTITY OF VIRUS OF SMALLPOX AND VACCINIA.

Robert Ceely thought that he had proved that he could inoculate a cow with smallpox, and produce a disease with a local vesicle, from which he could obtain virus; with this he tells us subsequently two thousand children were vaccinated without causing contagion in others. Chauveau and the Lyons Commission admit that he inoculated cows with the smallpox, but claim that the two thousand children were simply inoculated, and not vaccinated, and that the disease in them was contagious. It is a question of evidence: which is correct. Ceely is confirmed by Badcock's numerous experiments, and Chauveau is supported by Fleming, who, however, has no original experiments to offer, and is opposed in his conclusions by Professor Simmons, an equally reliable authority in veterinary matters. The Lyons Commission seems not to have been acquainted accurately with the English researches on this subject, and make many statements at direct variance with them on very slight proof. Ceely and Badcock found it *very difficult* to inoculate the cow; only about one out of thirty animals took. They obtained a well defined local vesicle, but no general eruption. Cows so inoculated failed to give the disease to others stalled with them. Badcock's experiments were made on over three hundred cows; Ceely's on a less number, but were carefully recorded and illustrated by colored plates from paintings taken on the spot. Badcock's virus has been used on over forty thousand persons, and Ceely's on a very large number, and both, after forty years, are still in use in England.

The French experimenters claim to have succeeded in *every* animal that they operated on, viz., twelve cows and three horses. The disease that they produced consisted in small vesicles scattered under the hair of the body around the seat of inoculation, and in their first five cases escaped recognition until subsequent experiments had taught them what to look for. They seem to have got no well marked vesicle at the point of inoculation, but rather an ill defined sore with small vesicles around it. With *matter* taken from this *sore* by scraping, they inoculated a number of children and produced a general eruption, which was contagious, and which caused the death of a child with the symptons of confluent smallpox.

Can we throw any light on this great difference in reported facts? We think recent researches help to explain, to some extent, this matter. First we may say that positive facts, from carefully conducted experiments on a sufficiently large number of animals, by competent experimenters, cannot

be overthrown by simply negative evidence on a much smaller number. The disease observed by the French experimenters did not resemble in any respect the disease described by Ceely and Badcock, as well as by several continental experimenters, either in appearance, period of incubation, or in the nature of the virus produced. It may be remarked that the descriptions of Ceely are almost classical in clearness, while the account of the experiments reported by Chauveau are unsatisfactory on many important points. English authors claim, with some show of reason, that smallpox matter, in an advanced stage, was placed in cuts and caused sores, but failed to affect the system of the cow. Simmons states that he and Marson made many experiments, and failed in producing smallpox in the cow; he, therefore, does not believe that the French Commission could have so uniformly succeeded, as they claim to have done; and he denies that they produced the smallpox at all in the cows that they experimented on, but claims that they simply introduced the virus into cuts, and caused a local irritation, and subsequently removed and used this matter to inoculate children. That they blundered, and that fatally; that the general eruption observed was either caused by irritation, or was of the nature of eczema; and that the short period of incubation would favor this explanation.

BUIST'S RESEARCHES.

Buist has shown that spores of vaccine and variola microbes measure but .15 μ (micromillimeters), while the microbes are much larger, as seen in cultivations of the clear lymph in the form of white, yellow, orange, or brown vaccine, or in the cloudy virus in the mature vesicle. When he vaccinated a monkey with the clear virus containing the spores alone, he produced a local vesicle, well defined, with slight constitutional disturbance; but when he used the developed forms of the microbe, as found in the colored vaccines, he got secondary vesicles also on other parts of the body.

Jenner believed that in vaccination he produced smallpox, but that the disease, owing to the previous passage of the virus through the cow's system, had lost its virulence and contagiousness. This change Pasteur calls attenuation of the virus. Buist says that perfectly fresh, transparent virus contains spores alone, whether vaccine or variolous, and that opaque lymph is only a natural cultivation of the spores into microbes, and that while the clear lymph is alkaline, the cloudy is acid, and that the action of these two lymphs is very different—the clear, as we have already said, acting with little local or constitutional irritation, while the cloudy causes ulceration and secondary vesicles.

He believes the spores are able to reproduce themselves by bursting, while the microbe multiplies by division as well. When the spores are inoculated they remain for a time at the place of introduction without causing irritation, and are gradually taken up by the lymphatics probably, and in them it may be the greater number of spores become developed into microbes and affect the system. The beginning of local irritation he believes indicates the development of microbes on the skin and their propagation of spores, which in their subsequent development effects rapid changes in the tissues by the withdrawal of something from them, by imparting something to them, and thus altering their actions. He failed to propagate spores in solid media, though he gives credit to Quist for having succeeded in Koch's culture fluid. He believes that instead of trying to improve our stock of virus by energizing that already in use, we should rather endeavor to mitigate by artificial culture variolous virus, using only

virus taken in the papular stage of the disease, before clouding has occurred. Both diseases he believes true fermentations. All fermentations he considers due to the development of spores into microbes, and to their propagation causing certain chemical changes, as the decomposition of sugar into alcohol and carbonic acid, which goes on until the sugar is used up, but may be started by a fresh supply; therefore, the microbes apparently are still alive, though dormant for a time. He finds that by inoculating dried yeast he can produce, after a certain time, a local sore, and he finds the yeast spore in the blood. In the monkey, vaccination did not fully protect it from smallpox inoculation, but after the additional yeast inoculation the protection was complete. By itself it modified the disease, though it did not prevent the entire formation of vesicles.

To return then to Ceely's experiments. He states that he used only perfectly limpid lymph in his inoculations of cows. Chauveau used the cloudy virus. It does not seem to me disproved by any experiment that has been recorded that cows cannot be so inoculated by smallpox virus as to have an eruption entirely different from the typical local vesicle obtained by Ceely. Indeed Buist's experiments would go to show that certain kinds of variola virus might produce a more general eruption than obtained by Ceely, Badcock, and others. If virus, at a late stage, containing microbes, not spores, be used, we should look for a general eruption. In the monkey neither the primary nor secondary vesicles caused the disease in other animals in the same cage. He does not, however, account for the well marked contagiousness of variolous inoculations in man, even when made with the virus taken perfectly clear from papules. He evidently believes that the cow's system attenuates the virus, and suggests its attenuation outside the body by suitable methods, as dilution (Salmon), or prolonged exposure to air (Pasteur). He, however, records no experiments on man; and, while his researches go to show how the Lyons Commission may have obtained a general eruption, they do not (as their object was different) prove conclusively the identity of the two viruses, though they tend to confirm what I at least consider as fully proved by evidence, the creditability of which I cannot doubt, and which has been so ably presented by Robert Ceely, viz., that cowpox is, in the cow as in man, only a modified smallpox, and that Jenner was perfectly accurate in speaking of the *vaccinæ variolæ*—the cow smallpox—and it is to be noted he refused to use any other name, apparently thinking that it might encourage the idea that vaccinia is an independent disease.

GENERAL CONCLUSIONS.

1. Vaccination is the artificial growth of a ferment on the skin, the products of which are absorbed and grow in the blood until the whole of the blood is affected, after which it is impossible, for a time at least, to repeat the process in the same person, who is then said to be protected. (Buist.)

2. The cause of this fermentation is due to the development of a microbe closely allied in all probability to yeast. This microbe is found in various stages of growth—as a spore, when the virus both in and out of the body is alkaline; in more mature forms, as found in the white or cloudy virus, seen after the areola forms or in old stored virus, and also in cultivations in solid media when the reaction is acid. We find varied forms or stages of growth of the microbe, which are indicated by characteristic colors, and which are able to reproduce themselves. These are, as named from their color, white, yellow, orange, and brown.

3. This microbe inoculated as a spore multiplies on the skin and in the

interior of the body, and develops into more mature forms. In doing this it takes free oxygen from the cells, and without it, it cannot develop. The interior of the body has been proved to contain little oxygen in the free state and the protoplasm of the cells to require but a scant supply. If the spores are more active than the cells, they absorb oxygen and excrete a ptomaine which paralyzes, so to speak, the functions of the cells. A ptomaine has been produced in the case of hog cholera outside of the body by the culture of the specific microbe in a suitable medium and its subsequent destruction by heat. Such a solution produces the disease when injected under the skin. The spores exhausting the oxygen of the cells in their development are rendered dormant or destroyed, and this terminates the disease. (Salmon.)

4. The microbe of smallpox and vaccinia are the same. This is proved by the inoculations of cows by Ceely and Badcock, and their conclusions are not in my opinion disproved by the experiments of Chauveau, and the arguments of Fleming and others. Though the microbe is the same in these two diseases, it is rendered probable by the experiments of Buist that their stage of growth is different. It will be remembered that he made cultivations from different vaccine vesicles and obtained four if not five kinds of virus characterized by their colors, viz., white, yellow, orange, and brown, besides the opaque found in the late vesicles. He also found that any one of the first four would produce a general eruption but no local vesicle, but if all four were inoculated a vesicle was also formed. He obtained similar colored viruses from variola. A single cultivation of the clear variola virus, taken early from papules, caused a modified action, as shown when inoculated on a monkey, while a second cultivation rendered its action still lighter and the monkeys both failed to give the disease by infection.

5. The only suitable material for vaccination is that containing spores alone, and not other developmental stages of growth of the microbe. Spores produce a typical vesicle, and no general eruption. Microbes in all their other stages cause great local irritation and often a general eruption. To this cause, doubtless, may be attributed the not uncommon eruptions that were found to follow vaccination with certain animal viruses during the recent prevalence of smallpox in this State.

6. All authorities are agreed that arm-to-arm or calf-to-arm vaccination is that most certain to produce typical vesicles in the greatest proportion of cases, and without undue local irritation or general eruption. Of all stored lymph, that preserved by drying *thoroughly* and *quickly* keeps best and preserves the spores in the spore state, but it requires special skill in using to remove the virus from the points, and to introduce it into the skin.

RULES FOR THE USE OF ANIMAL VIRUS.

The following rules are the result of the most recent research, and may, perhaps, be found convenient to the reader:

1. Only vaccinate those free from fever or skin eruptions, except when absolutely necessary.

2. Cleanse the arm with soap and water and rub until red.

3. Moisten the point in lukewarm water or glycerine and water, and mix the virus on it with the moisture with another point.

4. Apply the virus to the part to be vaccinated, and scratch the skin through it with the point or with a needle, or abrade the skin first with the sharp sides of the point, and then apply the virus. In either case, it is better to make two vaccinations at a distance of an inch and a half from

each other, and each at least one quarter of an inch square. The virus must be *rubbed* in well. *Whatever instrument is used it should never be used for another case.*

5. See that the vesicle is not injured. Apply, if necessary, jewelers' cotton and a bandage over it, if there is any danger of exposure to infection, dust, or cold.

6. See cases in one week; give only provisional certificates until results are known with certainty.

7. Keep animal virus dry and cool. The temperature should be steady and not over 60 degrees. This may generally be done by wrapping in gutta percha tissue, and putting in a wide-mouthed jar, in which is a small uncorked wide-mouthed bottle containing unslacked lime, closing securely the jar and keeping it in the cellar. Virus will often become inactive in a few hours if exposed to moisture together with sudden changes of temperature.

8. Virus apparently inactive will often become active if wet with glycerine and water, and the virus well mixed with it and allowed to stand under cover for several hours in a warm room before using.

9. Examine all points after using by pouring water over them to see that the virus is all removed.

10. Lastly, take plenty of time, use enough virus, and be sure that it is well rubbed in, and the scarification dry before you dismiss the patient.

NOTE.—Animal virus that produces in any considerable proportion of cases local ulcerations, much fever, and secondary eruptions, if free from septic material, is a virus containing the mature forms of the microbe, and not the spores alone. It is usually propagated by large abrasions in adult animals, which give an enormous yield of liquor sanguinis, with microbes in different stages of development in it, and frequently pus and the results of inflammatory action also. It is very active locally and constitutionally, but is not a pure virus. It is responsible for many of the accidents that sometimes attend this operation. All authorities are agreed that pure animal virus, *i. e.*, virus containing spores alone, acts with little irritation, and that its course is slower than long humanized virus. Virus is never to be judged by the violence of its action, either locally or constitutionally, but rather by its action conforming to a Jennerian type.

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